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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/852,020	05/06/97	MARUYAMA	I

HM12/0223
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EXAMINER	
LEFFERS JR,G	
ART UNIT	**PAPER NUMBER**
1636	26

DATE MAILED: 02/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.	Applicant(s)
08/852,020	Maruyama, et al
Examiner	**Group Art Unit**
Gerald G. Leffers Jr.	1636

THE PERIOD FOR RESPONSE: [check only a) or b)]

a) ☐ expires _____ months from the mailing date of the final rejection.

b) ☐ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☒ Appellant's Brief is due two months from the date of the Notice of Appeal filed on *Jan 18, 2001* (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on *Jan 18, 2001* has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:

☒ The proposed amendment(s):

☒ will be entered upon filing of a Notice of Appeal and an Appeal Brief.

☐ will not be entered because:

☐ they raise new issues that would require further consideration and/or search. (See note below).

☐ they raise the issue of new matter. (See note below).

☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: _____

☐ Applicant's response has overcome the following rejection(s):

_____

☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.

☒ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:

The arguments regarding enablement are not persuasive (see attachment). Rejection of the claims for lack of written description has not been addressed.

☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):

Claims allowed: _____

Claims objected to: _____

Claims rejected: *57-60*

☐ The proposed drawing correction filed on _____ ☐has ☐has not been approved by the Examiner.

☐ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). _____.

☐ Other

Attachment to Advisory Action

Receipt is acknowledged of the Terminal Disclaimer, After-Final amendment and Notice of Appeal filed 1/18/01. The Terminal Disclaimer over U.S. Patent No. 5,627,024 is proper and has been entered into the file.

The amendment of claim 57 will be entered into the file upon filing of an Appeal Brief. Amendment of claim 57 in the After-Final amendment of 1/18/01 merely overcomes a rejection of claim 57 under U.S.C. 35 112, second paragraph, as being vague and indefinite. This amendment does not address the remaining issues under 35 U.S.C. 112, first paragraph. Applicants' response in the After Final amendment of 1/18/01 does not even address rejection of claims 57-60 under 35 U.S.C. 112, first paragraph, for lack of written description. The arguments regarding rejection of the same claims for lack of enablement under 35 U.S.C. 112, first paragraph, have been considered but are not deemed persuasive.

Applicants' response essentially argues: 1) a skilled artisan need only produce an expression vector in accordance with the claimed instructions, 2) it is well within the ordinary skill in the art to determine on which terminus of a polypeptide resides its biological activity for the purpose of identifying where to attach a linker to the polypeptide (e.g. N or C terminus) and it is well within the skill of the art to determine the appropriate size of such a linker, 3) the post-application Mikawa reference demonstrates the instant specification was in fact enabling, 4)the fact that Mikawa was not named an inventor of the instant application demonstrates that persons of ordinary skill in the art (not the inventors) can practice the claimed invention based upon the

teachings of the instant application, and 5) the use of conditional suppression or conditional fusion as set forth in the present disclosure and claims minimizes concerns about phage disruption.

Simply producing a vector having the recited functional elements is not enough if one of skill in the art is to practice the invention such that the resulting phage displays the fusion polypeptide in a manner wherein the phage is assembled and in such a manner that the desired polypeptide is displayed in an accessible, active conformation on the assembled phage. Regarding the assertions that it is well within the skill of the art to determine which portion of a protein has biological function such that a heterologous polypeptide may be inserted therein and with regard to determining an optimum linker between the matrix protein and the heterologous polypeptide, the examiner maintains for reasons of record that one cannot do so in a predictable fashion such that the experimentation required would be routine, predictable experimentation having a reasonable expectation of success. As noted in the previous Action, the prior art and the specification make no suggestion as to which portions of the matrix proteins other than pV might be dispensable for proper phage assembly and which also might appropriate for display of an attached heterologous polypeptide such that the polypeptide is displayed in an accessible, active conformation. For example, Mikawa et al states that the ends of pD are not involved in the interaction between pD subunits or between pD and pE subunits, "an important result for which no guarantee existed at the start of this work." (page 27, first paragraph of the Discussion). Mikawa et al is post-filing art. Therefor, given the state of the prior art and lack of teachings of

the specification regarding insertion of a heterologous polypeptide into one of the phage matrix proteins such that the phage 1) assembles properly and 2) assembles such that the heterologous polypeptide is displayed in an active, accessible conformation, it would have been unpredictable whether an insertion of a heterologous polypeptide in any part of any of the other matrix proteins would allow assembly of a phage bearing the heterologous polypeptide in an active, accessible form. Regarding the assertion that the fact that Mikawa was not named as a co-inventor demonstrates one of ordinary skill in the art could, based upon the specification, make and practice the claimed invention, this assertion is not relevant absent any indication of the exact nature of the contributions of Mikawa to the work described in Mikawa et al and any indication of whether Mikawa is actually "one of ordinary skill in the art". Finally, regarding the presence of the conditional suppression of expression for the fusion polypeptides on the surface of the phage, the examiner acknowledges that this allows for side-by-side comparison of phage assembly in suppressor and non-suppressor strains and that one can use such an assay to determine whether phage disruption occurred to any significant extent. The presence of an assay for determining the extent of disruption does not make the generation of such phage more predictable. Nor does such an assay address the secondary issue of whether the heterologous polypeptide is displayed in a manner such that it is accessible and in an active form. The examiner submits that the assertion that the present invention is merely routine in nature and within the repertoire of the skilled artisan is inaccurate for reasons of record and for the reasons stated above.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald Leffers, Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than 24 hours after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richard Schwartz, can be reached on (703) 308-1133.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

GLJr

G. Leffers, Jr.
Patent Examiner
Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER

February 14, 2001